REMARKS

Entry of the foregoing and reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested in light of the remarks which follow.

By the foregoing amendment, claims 35, 36, 38, 39, 40, and 41 are amended to recite sequence identifiers and address informal issues. Claim 40 is amended to clarify the nature of the pharmaceutical composition. Basis may be found throughout the specification, for example at page 8, line 6 (pharmaceutical carriers). Thus, no prohibited new matter is presented herein. Further to a telephone call with Examiner Mosher, Applicants note that a supplemental response will be provided, if necessary, addressing any further issues with regard to the sequence listing and sequence identifiers.

Information Disclosure Statement of May 31, 2001

The Office has requested copies of references BM (*Cytomedins* (Bulletin), "Peptide Bioregulators", April 13, 1990, Russia), BP (R.S.Chen, *Chemical Abstracts*, 111(7), Abst. No. 5523OR (1984), and CF (Hirschmann, *Chemical Abstracts*, 79 (11), Abst. No. 66820e (1973), from the Information Disclosure Statement filed on May 31, 2001, as the Office cannot readily locate them. These references will follow shortly.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 31-40 and 45-47 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly indefinite.

The Office states that claim 40 confuses the meaning of claim 31, as it is purportedly unclear as to how the method of treatment of claim 31 can be practiced without being in composition form as recited in claim 40. The composition of claim 40 is to be administered with an appropriate excipient/carrier. Thus, claim 40 is amended herein to clarify the nature of claim 40, reciting that the peptide having the formula R'-GlxLys-R" or a pharmaceutically acceptable salt thereof is in combination with a pharmaceutically acceptable carrier.

In light of the above, Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 31-47 stand rejected under 35 U.S.C. § 112, second paragraph, as purportedly failing to comply with the enablement requirement. Specifically, the Office states that while the specification is enabling for a method of augmenting vaccination in a fish, it does not provide sufficient enablement for augmenting a vaccination in any host. Applicants traverse, and submit that the specification, as well as what is known in the art, provide the skilled artisan with the ability to practice the claimed methods without undue experimentation.

To this end, the specification does provide examples with regard to mammals. Examples 1-4 report experiments with guinea pigs. The guinea pigs were treated with peptide preparations to determine the effects on the immune system. Examples

7-8 report experiments with mice, studying hemodepression and the efficacy of Glu-Lys. In any case, the absence of working examples will not by itself render the invention non-enabled. *See* M.P.E.P. § 2164.02.

In support of the comments in the Office Action, the Office has cited to Warr (Development in Biological Standardization 90:15-21, 1997) as showing that the immune systems of fish and mammals are different. Applicants note that while there are, of course, some differences between the immune systems of fish and mammals, the immune systems are in fact very similar. Fish and mammals appear to have the same basic immune structure as would be affected by the augmenting methods of the invention. For example, page 16 of Warr states that "...fish (above the level of agnatha) possess all the basic mechanisms and, in some form, the molecules of higher vertebrate immunity, that is to say, T cells, B cells, lymphocyte cooporation, antigen presentation, MHC, TCR, Igs, cytokines and accessory molecules." Thus, although fish and mammals do not have identical immune systems, their immune systems are the same with regard to the basic structure and components. Further, page 19 notes that "..it is clear that the chon-drich-thyan and osteichthyan fishes use the same basic biochemical machinery as the mammals for the recognition and effector phases of their adaptive immune responses." These similarities makes fish a useful experimental model. Thus, the skilled artisan could practice the present invention with regard to mammals without further experimentation. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom.*, and *See In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

With regard to the scope of the peptides used, Applicants submit that a variety of peptides are further discussed in the specification and can be shown to have immunomodulating activities. To this end, Applicants cite page 5 of the specification, setting forth structural and functional guidance as to the claimed peptides, as well as pages 6-7, discussing preferred substituents.

In light of the above remarks, Applicants request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 31, 34, and 40-47 stand rejected under 35 U.S.C. §103(a) as purportedly unpatentable over Nyeki (U.S. Patent No. 5,041,535) ("Nyeki"). The Office states that Nyeki discloses two immunostimulating peptides of less than 9 amino acids comprising DK residues, able to improve antibody production in immunosuppressed mice when administered after an immunizing antigen. However, Nyeki discloses the use of sheep erythrocytes as test antigen, instead of a vaccine.

For a *prima facie* case of obviousness, the following three requirements must be met. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine the reference with another reference. Second, the proposed modification must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. Third, the prior art reference must teach or suggest all the limitations of the claims. The teachings or suggestions, as well as the expectation of success, must come from the prior art and

not from applicant's disclosure. *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988); *Amgen, Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991); and *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991).

Applicants respectfully submit that the cited reference, does not meet the requirements for a *prima facie* case of obviousness. As recited in claim 1, the present invention is directed to a method for augmenting vaccinations in a host comprising: administering to said host a peptide having the formula R'-Glx-Lys-R" or a pharmaceutically acceptable salt thereof, wherein Glx is Glu or Gin; R' is LI- or a first amino acid sequence having 7 or fewer amino acids, wherein R" is -H or a second amino acid sequence having fewer than 7 amino acids; wherein said peptide has a sequence of at least 2 but not more than 9 amino acids; and administering to said host a vaccine.

In contrast, Nyeki discloses thymopoietine fragment analogs, which possess a strong antitumor effect. Nyeki does not disclose the administration of a vaccine. Instead, Nyeki is concerned with the anti-tumor effects of the disclosed peptide compositions. As Nyeki discloses the anti-tumor effect as being important, Nyeki provides no motivation to use a vaccine, nor any expectation of success.

Further, Applicants respectfully submit that the claims are patentable over the cited references because unexpected results are present with respect to the claimed methods.

It is a well established legal precedent that the presence of an unexpected, advantageous or superior result is evidence of nonobviousness. *See, e.g.,* M.P.E.P. § 716.02(a); *In re Papesch*, 315 F.2d 381, 137 U.S.P.Q. 43 (C.C.P.A. 1963). Along

these lines, it is also well established that "a greater than expected result" is evidence of nonobviousness. *See* M.P.E.P. § 716.02(a); *In re Corkill*, 711 F.2d 1496, 226 U.S.P.Q. 1005 (Fed. Cir. 1985).

As noted in the present specification, especially at pages 4-5, it is unexpected for such small compounds to have such broad range effectiveness and lack of side effects. The small peptide compositions of the present invention exhibit a broad range of efficacy for modulation of the immune system, and may be used in the prevention and treatment of infections in immunocompetant and immunosuppressed patients, and for the treatment of certain immune conditions, such as AIDS. Also unexpectedly, the present peptides do not exhibit any significant side effects, and also are inexpensive to make due to their small size.

In light of the above remarks, Applicants request that the rejections under 35 U.S.C. § 103 be withdrawn.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited

In the event that there are any questions relating to this Amendment and Reply, or the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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